REMARKS

I. Status of the Application and Claims

Claims 1-14 are rejected. Claims 15-42 have been added. Support for newly added claims 15-42 may be found throughout the specification and original claims. For example, claims 15-17 and 21 are supported in original claims 6 and 13. Support for claims 18-20 and 22-24 may be found, for example, in Table 1, on page 8 of the specification. Support for newly added claims 25-42 may be found at least on page 5 at lines 1-16, on page 10 at lines 6-15, and in the original claims. Claims 1-42 are under consideration.

II. Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 4 and 11 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter Applicant regards as the invention. Office Action, page 2. The Office alleges the term "acute" is undefined and the claims are unclear as to the appropriate dosage size of an acute dosage. *Id.*

The specification on page 3, lines 12-13, discloses that "acute" refers to a treatment that is administered while the patient is experiencing AECB. An "acute treatment", therefore, does not refer to a particular dosage administered, but rather to the timing of the treatment. In view of this disclosure, claims 4 and 11 are clear and definite. Applicant therefore respectfully requests the rejection be withdrawn.

III. Rejection under 35 U.S.C. § 102

Claims 1-5, 7-12, and 14 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Kim *et al.* (WO 98/42705) ("*Kim*"). Office Action, page 2.

According to the Office, *Kim* discloses gemifloxacin and its mesylate and sesquihydrate salts, and the use of gemifloxacin compounds to treat respiratory infections. Office Action, page 3. The Office concludes that because *Kim* teaches treating a respiratory infection, the claims are anticipated. *Id.*

The invention claimed, however, is not a method of treating any respiratory tract infection: the invention claimed is methods of reducing the recurrences or the severity of recurrences of acute exacerbations of chronic bronchitis (AECB) by administering gemifloxacin. A rejection under 35 U.S.C. § 102 is only proper when the claimed subject matter is identically described or disclosed in the prior art. *In re Arkley*, 455 F.2d 586, 587 (CCPA 1972); *see also* M.P.E.P. § 706.02(a) ("For anticipation under 35 U.S.C. 102, the reference must teach every aspect of the claimed invention either explicitly or impliedly."). Each and every element of a claim must be set forth in the prior art reference for there to be anticipation. *See* M.P.E.P. § 2131.

Kim does not teach each and every element of the claimed invention, either explicitly or impliedly. Recurrence of acute exacerbation of chronic bronchitis involves a discrete patient population suffering from chronic bronchitis. *See, e.g.*, Ball, *Epidemiology and Treatment of Chronic Bronchitis and Its Exacerbations*, Chest, Vol. 108, pages 43S-52S (1995) (previously provided on Form PTO-1449). Respiratory infections, in contrast, are not limited to patients with AECB. Treatment of a respiratory infection, therefore, does not necessarily involve treatment of a patient with AECB. "A

claim limitation is inherent in the prior art if it is necessarily present in the prior art, not merely probably or possibly present." *Akamai Technologies, Inc. v. Cable & Wireless Internet Serv., Inc.*, 344 F.3d 1186, 1192, 68 USPQ2d 1186, 1190 (Fed. Cir. 2003). Because treatment of a respiratory infection does not necessarily involve reducing the recurrences or the severity of recurrences of AECB, *Kim* does not anticipate the claimed invention. Applicant respectfully requests the rejection be withdrawn.

IV. Rejections under 35 U.S.C. § 103

A. *Kim* in view of *Sherlock*

Claims 1-14 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over the combination of Kim *et al.* (WO 98/42705) ("*Kim*") and Sherlock (U.S. Pat. No. 4,452,800) ("*Sherlock*") and knowledge in the art. Office Action, page 3.

The Office states that *Kim* teaches gemifloxacin and its use to treat respiratory diseases. Office Action, page 3. The Office acknowledges that *Kim* does not teach the particular dosage recited, but considers the recited dosage to be optimization based on *Kim*'s general disclosure of administering up to 400 mg. *Id.* at 4. The Office likewise considers the duration of the administration of gemifloxacin to be non-critical. *Id.* The Office cites *Sherlock* as teaching the use of 1,8-naphthyridine compounds to treat respiratory diseases such as bronchitis and pulmonary obstructions such as asthma. *Id.* The Office also points to various abstracts for support that gemifloxacin can be used treat the pathogens *H. influenza* and *S. pneumoniae*, which are pathogens associated with acute exacerbations of chronic bronchitis (AECB). *Id.* at 5. The Office concludes that given this knowledge, one of ordinary skill in the art would have been motivated to

use the compound taught by *Kim* to treat chronic respiratory and pulmonary disorders because of the compound's anti-bacterial effects, with the expected result of providing successful treatment regimes. *Id.*

In formulating its rejection of claims 1-14, the Office has not pointed to a reason why the ordinary artisan would have been motivated to substitute the antibiotic gemifloxacin for the anti-allergic1,8-naphthyridine compounds *Sherlock* teaches for use in treating chronic obstructive lung disease. To establish a *prima facie* case, the Office bears the burden of showing that:

> (1) . . . the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) . . . the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure.

In re Vaeck, 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991) (citations omitted). In addition, the combination of references must teach or suggest all of the claim limitations. *In re Royka*, 180 U.S.P.Q. 580, 583 (C.C.P.A. 1974).

Here the Office has relied upon a general teaching that gemifloxacin can possibly be used to treat respiratory disease, and concluded that because *Sherlock* teaches that 1,8-naphthyridine compounds can be used to treat bronchitis, gemifloxacin can also be used to "treat" AECB. However, "[t]he mere fact that references <u>can</u> be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination." M.P.E.P. § 2143.01 (citing *In re Mills*, 916 F.2d 680,16 USPQ2d 1430 (Fed. Cir. 1990)). The Office has not provided clear and particular reasons why the ordinary artisan would have been motivated to select

gemifloxacin, an antibiotic, substitute gemifloxacin for the anti-allergenic 1,8-naphthyridine compounds taught by *Sherlock*, then adapt the method of treating bronchitis taught by *Sherlock* to a method of reducing the recurrences or severity of recurrences in AECB.

Unlike gemifloxacin, which functions as an antibiotic and so kills bacteria or inhibits their growth, the 1,8-naphthyridine compounds taught by *Sherlock* act by inhibiting the release of mediators such as SRS-A (slow reacting substances of anaphylaxis) and histamine and antagonize the action of SRS-A on respiratory tissue. (Col. 1, lines 34-39.) *Sherlock* characterizes them as anti-allergy compounds. *Id.*, line 50. The compounds of *Sherlock* do not kill bacteria or inhibit their growth, but instead inhibit the inflammatory response of the patient. That the compounds of *Sherlock* and gemifloxacin have different mechanisms of action is unsurprising given the differences in their structures. *Sherlock* teaches that chronic obstructive lung disease can have allergic or non-allergic causes, and that the 1,8-naphthyridine compounds taught by *Sherlock* are useful for treating *allergic* chronic obstructive lung disease. (Col. 1, lines 39-44.) Thus, the ordinary artisan at the time the invention was made would not have considered a therapy that targeted an allergic reaction to be appropriate for use when the bronchitis was non-allergic, nor would the ordinary artisan have considered an antibacterial therapy appropriate when the bronchitis had an allergic cause. Given the different forms of bronchitis and the different mechanisms of action of gemifloxacin and the 1,8-naphthyridine compounds of *Sherlock*, the ordinary artisan would not have been motivated to substitute gemifloxacin for the 1,8-naphthyridine compounds of *Sherlock* to treat bronchitis. Neither has the Office set forth reasons why the ordinary artisan would

have been motivated to administer gemifloxacin not just to treat the general condition of bronchitis, but for reducing the recurrence or severity of acute exacerbations of chronic bronchitis. Finally, while the Office cites "knowledge in the art" as showing that gemifloxacin could treat pathogens associated with AECB, the Office again does not address why the ordinary artisan would have been motivated to replace antibiotics already in use for AECB therapy with gemifloxacin.

The Office has not provided clear and particular reasons why the ordinary artisan would have been motivated to combine the teachings of the references and knowledge in the art to arrive at Applicant's invention. Because the Office has not met its burden of establishing a *prima facie* case of obviousness, Applicant respectfully requests that the rejection as applied to claims 1-14 be withdrawn.

B. *Lowe* in view of *Grossman*

Claims 1, 4-6, 8, and 11-13 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over the combination of Lowe *et al.* (Drugs, Vol. 59, No. 5, pages 1137-47)) ("*Lowe*") and Grossman (Chest, Vol. 112, No. 6, suppl. pages 310S-13S) ("*Grossman*"). Office Action, page 5.

The Office cites *Lowe* for teaching the effectiveness of gemifloxacin against *H. influenzae*, *M. catarrahalis*, and other respiratory pathogens, and for the use of a dosage of 320 mg/day in clinical trials. Office Action, page 5. The Office states that *Lowe* does not teach a specific method for treating AECB, but that *Grossman* teaches treatment of *H. influenzae* with antibiotics. *Id.* at 6. According to the Office, the skilled artisan would have followed the teachings of *Grossman* to treat pathogens associated with AECB with antibiotics, and applied the knowledge of *Lowe* that gemifloxacin is

effective against these pathogens. *Id.* The Office considers it an expected result that gemifloxacin could be used to treat AECB, and views the best interests of the patient as providing sufficient motivation for the selection of gemifloxacin as the antibiotic for use in treating AECB. *Id.*

The requirements for establishing a *prima facie* case of obviousness have been discussed *supra*. As in the rejection based on the combination of *Kim* and *Sherlock*, the Office has again failed to provide clear reasons why the ordinary artisan at the time the invention was made would have been motivated to select gemifloxacin from among known antibiotics to replace the treatment taught by *Grossman* for AECB. Applicant once again points out that "[t]he mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination." M.P.E.P. § 2143.01 (citing *In re Mills*, 916 F.2d 680,16 USPQ2d 1430 (Fed. Cir. 1990)).

Because the Office has not established why it would be not just possible, but also desirable, to substitute gemifloxacin at the recited dosages and for the recited course of therapy in the methods of *Grossman*, the Office has not established a *prima facie* case. Applicant therefore respectfully requests the rejection be withdrawn.

V. Conclusion

In view of the foregoing remarks, Applicant respectfully requests reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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